Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

CAS Number: 64604-2

F1_M3

C Number: C20008

Lock Date: 06/29/2006

Cage Range: ALL

Date Range: ALL

Reasons For Removal: ALL

Removal Date Range: ALL

Treatment Groups: Include ALL

Study Gender: Both

TDMSE Version: 2.0.0

Date Report Requested: 09/30/2008

Time Report Requested: 13:13:48
First Dose M/F: 03/25/03 / 03/25/03

Test Type: CHRONIC

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

Lab: SRI

Species/Strain: MICE/B6C3F1

B6C3F1 MICE MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Disposition Summary				
Animals Initially in Study	50	50	50	50
Early Deaths Moribund Sacrifice		1	1	1
Natural Death	5	3	6	•
Survivors Terminal Sacrifice	45	46	43	49
Animals Examined Microscopically	50	50	50	50 50
ALIMENTARY SYSTEM				
Intestine Large, Cecum	(48)	(47)	(49)	(50)
Adenoma Intestine Small, Ileum	(49)	1 (2%) (48)	(50)	(50)
Intestine Small, Jejunum	(49)	(49)	(46)	(50)
Carcinoma		1 (2%)	1 (2%)	, ,
Liver Alveolar/Bronchiolar Carcinoma,	(50)	(50) 1 (2%)	(50) 1 (2%)	(50)
Metastatic, Lung		I (Z70)	I (∠70)	
Cholangiocarcinoma			1 (2%)	
Hemangiosarcoma		1 (2%)	1 (2%)	1 (2%)
Hepatoblastoma Hepatocellular Adenoma	7 (14%)	1 (2%) 11 (22%)	5 (10%)	
Hepatocellular Adenoma, Multiple	5 (10%)	2 (4%)	0 (1070)	1 (2%)
Hepatocellular Carcinoma	13 (26%)	13 (26%)	12 (24%)	7 (14%)
Hepatocellular Carcinoma, Multiple Sarcoma	4 (8%)	2 (4%) 1 (2%)	2 (4%)	
Mesentery	(2)	(3)	(3)	(3)
Alveolar/Bronchiolar Carcinoma,	\ - /	(-)	1 (33%)	(-)
Metastatic, Lung				4 (220()
Carcinoma, Metastatic, Islets, Pancreatic Hemangioma	1 (50%)			1 (33%)
Hemangiosarcoma	1 (3070)	1 (33%)		
Pancreas	(49)	(49)	(49)	(50)
Cholangiocarcinoma, Metastatic, Liver	(50)	(50)	1 (2%)	(50)
Salivary Glands Stomach, Forestomach	(50) (50)	(50) (50)	(50) (50)	(50) (50)

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

Lab: SRI

Species/Strain: MICE/B6C3F1

B6C3F1 MICE MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Stomach, Glandular Sarcoma	(49)	(50) 1 (2%)	(50)	(50)	
CARDIOVASCULAR SYSTEM					
Heart Alveolar/Bronchiolar Carcinoma, Metastatic, Lung	(50)	(50)	(50) 1 (2%)	(50)	
ENDOCRINE SYSTEM					
Adrenal Cortex Adenoma Capsule, Adenoma Adrenal Medulla Pheochromocytoma Benign Islets, Pancreatic Adenoma Carcinoma Parathyroid Gland Pituitary Gland Thyroid Gland Follicular Cell, Adenoma	(50) 1 (2%) (49) 1 (2%) (49) (50) (48) (48)	(50) 1 (2%) (50) (49) 1 (2%) (50) (48) (49) 1 (2%)	(50) 4 (8%) 1 (2%) (49) (49) 1 (2%) (50) (47) (50)	(50) 3 (6%) (49) (50) 1 (2%) 1 (2%) (50) (50) (50)	
GENERAL BODY SYSTEM					
Tissue NOS Hemangiosarcoma	(0)	(0)	(0)	(1) 1 (100%)	
GENITAL SYSTEM					
Epididymis Preputial Gland Adenoma	(50) (50) 1 (2%)	(50) (50)	(50) (50)	(50) (49)	
Carcinoma Prostate Seminal Vesicle Testes	(50) (50) (50)	(50) (50) (50)	1 (2%) (50) (50) (50)	(50) (50) (50)	

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

Lab: SRI

Species/Strain: MICE/B6C3F1

B6C3F1 MICE MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Interstitial Cell, Adenoma	1 (2%)				
EMATOPOIETIC SYSTEM					
Bone Marrow	(49)	(49)	(49)	(50)	
Hemangiosarcoma Lymph Node	1 (2%) (2)	1 (2%) (1)	(2)	(0)	
Iliac, Sarcoma	(2)	1 (100%)	(2)	(0)	
Mediastinal, Alveolar/Bronchiolar		,	1 (50%)		
Carcinoma, Metastatic, Lung			4 (500/)		
Mediastinal, Carcinoma, Metastatic, Lung Lymph Node, Mandibular	(48)	(45)	1 (50%) (49)	(47)	
Sarcoma	(40)	1 (2%)	(40)	(47)	
Lymph Node, Mesenteric	(47)	(44)	(48)	(48)	
Hemangioma	1 (2%)	(==)	(12)	()	
Spleen Hemangiosarcoma	(50)	(50) 3 (6%)	(49) 1 (2%)	(50)	
Sarcoma	2 (4%)	3 (6%) 1 (2%)	1 (2%)	1 (2%)	
Thymus	(45)	(46)	(49)	(40)	
Carcinoma, Metastatic, Lung	, ,	, ,	1 (2%)	<i>、,</i>	
NTEGUMENTARY SYSTEM					
Skin	(50)	(50)	(50)	(50)	
Squamous Cell Carcinoma		()	1 (2%)	(/	
Sebaceous Gland, Carcinoma	1 (2%)				
Subcutaneous Tissue, Fibrona	1 (2%)			1 (20/)	
Subcutaneous Tissue, Fibrosarcoma Subcutaneous Tissue, Fibrous	2 (4%)	2 (4%)	1 (2%)	1 (2%)	
Histiocytoma	2 (170)	2 (170)	1 (270)		
Subcutaneous Tissue,	2 (4%)				
Hemangiosarcoma					
IUSCULOSKELETAL SYSTEM					
Bone	(50)	(50)	(50)	(49)	
Skeletal Muscle	`(1) [′]	(2)	(1)	(0)	
Alveolar/Bronchiolar Carcinoma,			1 (100%)		
Metastatic, Lung					

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48

First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

B6C3F1 MICE MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Hemangiosarcoma Sarcoma	1 (100%)	1 (50%)			
NERVOUS SYSTEM					
Brain Peripheral Nerve	(50) (1)	(50) (1)	(50) (1)	(50) (1)	
RESPIRATORY SYSTEM					
Lung Alveolar/Bronchiolar Adenoma Alveolar/Bronchiolar Adenoma, Multiple	(50) 1 (2%)	(50) 1 (2%) 1 (2%)	(50) 4 (8%)	(50) 2 (4%)	
Alveolar/Bronchiolar Carcinoma Alveolar/Bronchiolar Carcinoma, Multiple Carcinoma, Metastatic, Skin Carcinoma, Multiple	7 (14%) 3 (6%)	4 (8%) 2 (4%)	3 (6%) 1 (2%) 1 (2%)	7 (14%)	
Hepatocellular Carcinoma, Metastatic, Liver	4 (8%)	4 (8%)	1 (2%) 3 (6%)	1 (2%)	
Sarcoma	1 (2%)	1 (2%)			
SPECIAL SENSES SYSTEM					
Eye Harderian Gland Adenoma Carcinoma	(50) (50) 5 (10%)	(50) (50) 4 (8%) 2 (4%)	(50) (50) 7 (14%)	(50) (50) 5 (10%) 1 (2%)	
JRINARY SYSTEM					
Kidney Alveolar/Bronchiolar Carcinoma, Metastatic, Lung	(50)	(50) 1 (2%)	(50)	(50)	
Urinary Bladder	(50)	(50)	(49)	(50)	
SYSTEMIC LESIONS					
Multiple Organs	*(50)	*(50)	*(50)	*(50)	

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 09/30/2008

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

B6C3F1 MICE MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Lymphoma Malignant	6 (12%)		1 (2%)	2 (4%)	

a - Number of animals examined microscopically at site and number of animals with lesion

^{*} Number of animals with any tissue examined microscopically

Test Type: CHRONIC

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract **CAS Number:** 84604-20-6 Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

Lab: SRI

Species/Strain: MICE/B6C3F1

B6C3F1 MICE MALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Tumor Summary for Males				
Total Animals with Primary Neoplasms (b)	39	33	31	26
Total Primary Neoplasms	68	63	49	34
Total Animals with Benign Neoplasms	21	19	16	11
Total Benign Neoplasms	25	23	22	12
Total Animals with Malignant Neoplasms	29	24	24	19
Total Malignant Neoplasms	43	40	27	22
Total Animals with Metastatic Neoplasms	4	5	7	2
Total Metastatic Neoplasms	4	6	12	2
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

*** END OF MALE ***

a - Number of animals examined microscopically at site and number of animals with lesion b - Primary tumors: all tumors except metastatic tumors

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48

First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

B6C3F1 MICE FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
Disposition Summary				
Animals Initially in Study	50	50	50	50
Early Deaths				
Accidently Killed	_		_	1
Moribund Sacrifice	3	2	2	3
Natural Death Survivors	7	5	6	1
Natural Death		1		
Terminal Sacrifice	40	42	42	45
Animals Examined Microscopically	50	50	50	50
, ,				
ALIMENTARY SYSTEM				
Intestine Large, Cecum	(48)	(48)	(49)	(50)
Intestine Small, Duodenum	(49)	(47)	(47)	(49)
Intestine Small, Ileum	(46)	(49)	(48)	(49)
Intestine Small, Jejunum	(49)	(45)	(48)	(49)
Liver	(50)	(50)	(50)	(50)
Hemangiosarcoma	0 (00()	1 (2%)	4 (004)	
Hepatocellular Adenoma	3 (6%)	1 (2%)	4 (8%)	4 (00/)
Hepatocellular Carcinoma Mesentery	(5)	1 (2%)	(1)	4 (8%)
Hemangiosarcoma	(5)	(2)	(1) 1 (100%)	(3)
Osteosarcoma, Metastatic, Bone	1 (20%)		1 (10070)	
Oral Mucosa	(0)	(0)	(1)	(0)
Squamous Cell Carcinoma			1 (100%)	
Pancreas	(49)	(48)	(49)	(50)
Salivary Glands	(50)	(50)	(49)	(50)
Stomach, Forestomach	(50)	(50)	(50)	(50)
Squamous Cell Papilloma Stomach, Glandular	1 (2%)	(40)	1 (2%)	(EO)
Stomacn, Glandular Carcinoma	(50)	(48) 1 (2%)	(50)	(50)
Sarcoma Stromal, Metastatic, Uterus		1 (2/0)	1 (2%)	
CARDIOVASCULAR SYSTEM				
Heart	(50)	(50)	(50)	(50)

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Der: 84604-20-6 Firs

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

Lab: SRI

B6C3F1 MICE FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Sarcoma, Metastatic, Skeletal Muscle				1 (2%)	
ENDOCRINE SYSTEM					
Adrenal Cortex Adrenal Medulla Pheochromocytoma Benign Islets, Pancreatic Adenoma Parathyroid Gland Adenoma Pituitary Gland Pars Distalis, Adenoma Pars Intermedia, Adenoma Thyroid Gland Follicular Cell, Adenoma	(50) (49) (49) (48) (49) 2 (4%) (50)	(50) (49) 1 (2%) (48) 1 (2%) (48) (49) 2 (4%)	(50) (50) (49) 1 (2%) (48) (48) 1 (2%) 1 (2%) (49)	(50) (50) 1 (2%) (50) 1 (2%) (48) 1 (2%) (48) 2 (4%) (50) 1 (2%)	
GENERAL BODY SYSTEM Tissue NOS Alveolar/Bronchiolar Carcinoma, Metastatic, Lung Schwannoma Malignant	(0)	(1) 1 (100%)	(0)	(1) 1 (100%)	
GENITAL SYSTEM Clitoral Gland Ovary Cystadenoma Hemangioma Luteoma Uterus Hemangiosarcoma Polyp Stromal Sarcoma Stromal	(47) (46) 1 (2%) (50) 4 (8%)	(47) (50) 1 (2%) (50) 1 (2%) 1 (2%)	(49) (48) 1 (2%) 1 (2%) (50) 4 (8%) 1 (2%)	(47) (49) 1 (2%) (50) 1 (2%)	

HEMATOPOIETIC SYSTEM

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

B6C3F1 MICE FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Bone Marrow	(50)	(50)	(50)	(50)	
Hemangiosarcoma	()	2 (4%)	()	1 (2%)	
Lymph Node	(10)	(4)	(6)	(4)	
Iliac, Liposarcoma, Metastatic, Skin	, ,		2 (33%)	, ,	
Inguinal, Liposarcoma, Metastatic, Skin			2 (33%)		
Mediastinal, Hemangiosarcoma	1 (10%)				
Renal, Liposarcoma, Metastatic, Skin			1 (17%)		
Lymph Node, Mandibular	(48)	(49)	(46)	(47)	
Hemangiosarcoma	1 (2%)	>	(15)	(==)	
Lymph Node, Mesenteric	(49)	(47)	(49)	(50)	
Sarcoma Stromal, Metastatic, Uterus	(=0)	(40)	1 (2%)	(=0)	
Spleen	(50)	(48)	(49)	(50)	
Hemangiosarcoma	(40)	3 (6%)	1 (2%)	1 (2%)	
Thymus	(49)	(47)	(46)	(49)	
Sarcoma, Metastatic, Skeletal Muscle				1 (2%)	
NTEGUMENTARY SYSTEM					
Mammary Gland	(50)	(50)	(50)	(50)	
Carcinoma	(50)	2 (4%)	(30)	(50)	
Skin	(50)	(50)	(50)	(50)	
Subcutaneous Tissue, Fibrosarcoma	3 (6%)	1 (2%)	(00)	1 (2%)	
Subcutaneous Tissue, Fibrosarcoma,	0 (070)	1 (2%)		. (270)	
Multiple		. (= /3)			
Subcutaneous Tissue, Fibrous				1 (2%)	
Histiocytoma				. (=/5)	
Subcutaneous Tissue, Hemangioma	1 (2%)				
Subcutaneous Tissue,	,	1 (2%)			
Hemangiosarcoma		,			
Subcutaneous Tissue, Liposarcoma			2 (4%)	1 (2%)	
IUSCULOSKELETAL SYSTEM					
Bone	(50)	(FO)	(FO)	(50)	
Osteosarcoma	(50) 1 (2%)	(50)	(50)	(50)	
Skeletal Muscle	(3)	(2)	(0)	(3)	
Alveolar/Bronchiolar Carcinoma,	(3)	1 (50%)	(0)	(3)	
Metastatic, Lung		1 (30 /0)			
Hemangiosarcoma				1 (33%)	
i iemangiosarcoma				1 (33/0)	

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 09/30/2008

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

B6C3F1 MICE FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Liposarcoma, Metastatic, Skin Rhabdomyosarcoma Sarcoma	1 (33%)	1 (50%)		1 (33%) 1 (33%)	
IERVOUS SYSTEM					
Brain Peripheral Nerve Spinal Cord	(50) (3) (3)	(50) (0) (0)	(50) (0) (0)	(50) (0) (0)	
ESPIRATORY SYSTEM					
Lung Alveolar/Bronchiolar Adenoma Alveolar/Bronchiolar Carcinoma Carcinoma, Metastatic, Harderian Gland Carcinoma, Metastatic, Mammary Gland	(50) 1 (2%) 1 (2%)	(50) 2 (4%) 4 (8%) 1 (2%)	(50) 1 (2%) 2 (4%)	(50) 1 (2%)	
Fibrosarcoma, Metastatic, Skin Liposarcoma, Metastatic, Skin Osteosarcoma, Metastatic, Bone Rhabdomyosarcoma, Metastatic, Skeletal Muscle	1 (2%)	1 (2%) 1 (2%)		1 (2%)	
Sarcoma, Metastatic, Skeletal Muscle Nose Carcinoma, Metastatic, Harderian Gland	(50)	(50) 1 (2%)	(50)	1 (2%) (50)	
PECIAL SENSES SYSTEM					
Eye Harderian Gland Adenoma Adenoma, Multiple Carcinoma	(50) (50) 6 (12%) 2 (4%)	(50) (50) 2 (4%) 1 (2%) 2 (4%)	(50) (50) 5 (10%) 5 (10%)	(50) (50) 6 (12%) 1 (2%)	
JRINARY SYSTEM					
Kidney Urinary Bladder	(50) (50)	(49) (50)	(50) (50)	(50) (50)	

a - Number of animals examined microscopically at site and number of animals with lesion

Test Type: CHRONIC

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Date Report Requested: 09/30/2008

Spec	cies/Strain	: MICE/B6C3F	∙1
_			

B6C3F1 MICE FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM	
Transitional Epithelium, Carcinoma			1 (2%)		
SYSTEMIC LESIONS					
Multiple Organs Histiocytic Sarcoma	*(50) 1 (2%)	*(50)	*(50)	*(50) 1 (2%)	
Leukemia Granulocytic Lymphoma Malignant	11 (22%)	13 (26%)	16 (32%)	1 (2%) 15 (30%)	

a - Number of animals examined microscopically at site and number of animals with lesion

^{*} Number of animals with any tissue examined microscopically

Test Type: CHRONIC

Species/Strain: MICE/B6C3F1

Route: DOSED FEED

P05: INCIDENCE RATES OF NEOPLASMS BY ANATOMIC SITE (SYSTEMIC LESIONS ABRIDGED) (a)

Milk thistle extract

CAS Number: 84604-20-6

Date Report Requested: 09/30/2008

Time Report Requested: 13:13:48 First Dose M/F: 03/25/03 / 03/25/03

Lab: SRI

B6C3F1 MICE FEMALE	0 PPM	12500 PPM	25000 PPM	50000 PPM
umor Summary for Females				
Total Animals with Primary Neoplasms (b)	32	33	34	31
Total Primary Neoplasms	41	46	48	45
Total Animals with Benign Neoplasms	18	11	18	15
Total Benign Neoplasms	19	12	20	16
Total Animals with Malignant Neoplasms	19	26	26	22
Total Malignant Neoplasms	22	34	28	29
Total Animals with Metastatic Neoplasms	1	5	5	2
Total Metastatic Neoplasms	2	6	9	5
Total Animals with Malignant Neoplasms Uncertain Primary Site				
Total Animals with Neoplasms Uncertain-Benign or Malignant				
Total Uncertain Neoplasms				

*** END OF REPORT ***

a - Number of animals examined microscopically at site and number of animals with lesion b - Primary tumors: all tumors except metastatic tumors